THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

December 17, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1060
Rockville, MD 20852

Re: Docket No. 00D-1538, Draft Guidance for Industry; 21 CFR Part 11; Electronic Records; Electronic Signatures, Validation

The R.W. Johnson Pharmaceutical Research Institute and the Janssen Research Foundation welcome the opportunity to provide our collective comments on the *Draft Guidance for Industry on Electronic Records; Electronic Signatures, Validation*.

We support FDA's intention to provide guidance on computer system validation. While much has been written on this topic over the years, it remains a complex undertaking that can baffle those new to the validation process.

Our perception is that many people are looking to FDA for concrete, specific guidance on what FDA expects for validation activities and deliverables. In its current form, we are concerned that readers of this draft guidance may not fully understand that this is a high-level discussion of "key validation principles", or that they should use the reference list to learn the details of how to develop validated computer systems. Many people may misinterpret the guidance as the concrete, specific list they are looking for and therefore be inclined to meet the letter and not the spirit of the guidance.

Based on our experience with computer system validation, we would like to offer several suggestions for clarifying the guidance so it more clearly reflects its purpose as a high-level summary of important validation concepts.

Our most critical observations are described below. A detailed list of additional comments is attached to this letter.

1. General Comment
   We have read the final CDRH guidance, *General Principles of Software Validation, Final Guidance for Industry and FDA Staff*, and believe that on the whole this is an excellent description of software validation concepts. We especially like the guidance's emphasis on software risk analysis and flexibility of validation approach based on risk, the categorization of testing as structural / functional / user and the description of each, and the discussion of validating off-the-shelf software. We would like to see the Part 11 validation guidance more closely aligned with the CDRH guidance. Perhaps the Part 11 validation guidance could be expanded by including additional concepts and text leveraged from the CDRH guidance, or perhaps the guidances could be combined for a consistent approach to validation across FDA (recognizing that there are differences between development of software for medical devices and computer system validation of pharmaceutical applications).

2. Section 5.4.2, "Software testing should include:"
   We recommend modifying this section to describe the major types of software testing as structural, functional and user-site. This will align this guidance with the CDRH *General Principles of Software Validation* guidance as well as with common industry practice.

00D-1538

C 11

3. Section 5.6, Extent of Validation
We agree that the extent of validation for a particular system should be based on risk analysis of the system relative to product safety, efficacy and quality, data integrity, system complexity, etc. We recommend expanding this section and moving it to the beginning of Section 5, Key Principles, to emphasize that validation activities for a particular system should be chosen based on the risk analysis. The activities chosen may include those described in the guidance, or may include more or fewer activities, depending on the risk of the system. For any specific project the risk analysis and/or the validation plan should determine, justify, and document which validation activities will be performed.

4. Section 6.1.3, Functional testing of software (for commercial, off-the-shelf (COTS) software)
It is difficult to understand in this section exactly what FDA expects of the end-user (the company purchasing the software). It is especially important to understand FDA's expectations because we, like others in the pharmaceutical industry, are increasingly moving away from in-house system development and toward purchasing vendor-developed systems which are often highly customized, either by the vendor or the purchasing company.

   We believe that the testing activities for COTS software are essentially the same as for any software, regardless of how it is acquired. The differences lie in who does each type of testing, and in how the risk analysis is employed. We recommend reorganizing and clarifying the section as follows:

   - Revise section 5.4.2 as described in comment #2 above and apply these types of testing to COTS systems as well.
   - In section 6.1.3, state that for COTS systems, structural and functional testing are customarily performed by the vendor. User-site testing is performed by the end-user. The end-user should evaluate the software and the vendor using the considerations in 6.1.2. Depending on the results of the evaluation, and on the risk of the system, the end-user may or may not wish to perform (or repeat) portions of the structural or functional testing.
   - Remove "all" from the first sentence ("End users should conduct functional testing of software that covers all functions of the program that the end user will use.") to avoid the implication that the end-user *must* repeat *all* of the functional testing already performed by the vendor.
   - State that the ultimate responsibility for assuring adequate testing lies with the end-user.

Please refer to the attachment for additional comments. We hope that these comments will be useful to the Agency in developing the final guidance.

Sincerely,

The R.W. Johnson Pharmaceutical Research Institute

Mary Jean M. Link
Project Manager
Global Information Solutions Quality & Compliance

Janssen Research Foundation

Michael Weis
Director
Global Information Solutions Quality & Compliance

Attachment 1 – Additional Comments

1. Section 5.2.2 Validation Procedures
   Clarify that validation procedures are a set of documents that describe how the validation will be performed. As written, the section implies that validation procedures must be a single document. Consider using the wording from the CDRH guidance.

2. Section 5.2.2 Use of term "computer system configuration"
   Recommend adding a definition of "computer system configuration" to the Part 11 Glossary. Different people define "configuration" to different levels of detail, ranging from a high-level system description to a detailed list of hardware and software components. A definition would clarify FDA's expectations for the configuration description.

3. Section 5.2.3 Validation Report
   We agree that detailed documentation of test results is important, but detailed test results are often documented separately from the final validation report. The guidance should leave room for alternative approaches. Also, consider deleting the sentence about quantified test results. This concept is covered in Section 5.4.3.

4. Section 5.3 Equipment Installation
   Recommend changing "Prior to testing..." in the first sentence to "Prior to testing at the end-user's site..." to conform with current industry practice. While proper installation is important throughout the system development life cycle, it is most important prior to user-site testing to ensure that the manufacturer's specifications can be met in the user environment. Typically, installation is formally documented only during installation prior to user-site testing (and during installation in the production environment, if this is a separate environment).

5. Section 5.4.1, second bullet, Simulation tests
   We suggest expanding the description or referring readers to the reference list. As it is, the description is not complete enough for a reader inexperienced in testing techniques to understand. Such a reader may confuse it with a requirement for all validation projects. We assume simulation tests are mentioned as an example of a useful technique, not a requirement that must be done for every system in order for FDA to consider it validated.

6. Section 5.4.1, third bullet, Live, user-site tests
   As mentioned in our cover letter, we recommend moving this bullet to Section 5.4.2. We suggest leveraging additional text from the CDRH guidance to clarify and expand on the description of user-site testing. Clarify the second sentence: "Testing should cover continuous operations for a sufficient time ... in an effort to discover any latent faults...". While we agree with the importance of testing in the end-user environment under conditions that simulate production use, an inexperienced reader might think the sentence implies that finding all the latent faults is required. As stated in the CDRH guidance, "Software testing is very limited in its ability to surface all latent defects in software code."

7. Section 5.4.2, first bullet, Structural testing
   "Structural testing should show that the software creator followed contemporary quality standards...This testing usually includes inspection (or walk-throughs) of the program code and development documents." We disagree that the purpose of structural testing is to show that contemporary quality standards were followed. Similarly, structural testing does not customarily include code walkthroughs. We agree that following coding standards and code walkthroughs during development are important, for consistency with current industry practice we suggest moving this statement into a separate section on coding standards. The discussion of structural testing could also be improved by leveraging content from the CDRH guidance.

8. Section 5.4.2, third bullet, Program build testing
   The concepts in the description of program build testing belong more appropriately under the discussion of structural testing. We propose deleting this bullet and replacing it with the discussion of user-site testing, as suggested in earlier comments.

9. Section 5.4.3, How test results should be expressed
   Clarification of the term "quantifiable" is needed. It is not possible to express all test results in numerical form. User-site testing reproduces actual work processes and should test against user requirements, which are usually expressed in business language, not numerical terms. We believe pass/fail results are acceptable when expressing the passing or failing of an actual test result as compared to an expected test result. Expected results should be documented in some detail. We agree, for example, that it would be inappropriate for "Pass" to be recorded as the single result for an entire test script.

10. Section 5.5, Static verification techniques
    We agree that dynamic testing alone is not enough to "fully demonstrate complete and correct system performance". Quality must be built into the system via the use of an appropriate system development life cycle methodology. We believe this section could be improved by adding a discussion of the system development life cycle, design phase, and coding standards (as mentioned in comment #7 above). This section provides another opportunity to leverage content from the CDRH guidance.

11. Section 6.1, Use of phrasing "...by performing all of the following:"
    Sections 6.1, Commercial, Off-the-Shelf Software, and 6.1.2, Software Structural Integrity, contain wording to the effect of "End-users should ... perform *all* of the following" (emphasis added). We suggest removing the word "all" because it implies *all* the activities *must* be performed for *all* purchased systems. As stated in earlier comments, validation activities should be chosen for a particular system based on the risk analysis. While the approaches described in these sections are useful techniques, they may not be appropriate for all systems in all situations.